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Presentation Abstract

Session:	16-9-Arterial stiffness and disease - measurement, modelling and pathophysiology
Presentation:	Synchrotron Imaging of Angiotensin II-induced Abdominal Aortic Aneurysm in Mice
Location:	312
Presentation Time:	Thursday, Jul 10, 2014, 11:00 AM -11:18 AM

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Abstract: Abdominal aortic aneurysm (AAA) is often studied in angiotensin II-infused mouse models since these present many features that are also present in human AAAs, such as thrombus formation, medial elastolysis and a higher propensity for male gender. However, murine AAAs sometimes have a polymorphic or eccentric rather than a symmetric shape, are located suprarenally instead of infrarenally, and show rapid luminal growth that is preceded by a dissection of the medial layer. These findings have been documented in several labs but have never been fully understood, amongst others due to a lack of sufficiently detailed small animal imaging modalities. In this work murine AAAs have been provoked by a combined infusion of angiotensin II and anti-TGF-Beta antibodies in n=20 male normolipidemic C57BL6 mice (age 12 weeks) [1]. This mouse model leads to much more rupture-prone AAAs than the generally used angiotensin II infusion into hypercholesterolemic ApoE -/- mice. The animals were sacrificed at different stages of aneurysm development: n=12 intact AAAs were sacrificed 2 to 15 days after aneurysm induction and n=6 AAAs were obtained post mortem from animals that had died from aortic rupture. All AAA samples were flushed with PBS and kept in parafolmadehyde to be scanned ex-vivo with synchrotron-based X-ray tomographic microscopy (SRXTM) at the TOMCAT beamline of the Swiss Light Source of the Paul Scherrer Institute. Combining detailed soft tissue contrast provided by grating interferometry with anisotropic image resolution of 6.5 micron, the SRXTM images allowed us to describe aneurysm initiation, formation and rupture into unprecedented detail. We observed that angiotensin-provoked AAAs are not just preceded by but the consequence of a small dissection in the medial layer near the coeliac artery. This dissection leads to an intramural hematoma that is causing the rapid, and often eccentric expansion of the aortic lumen. The increased intramural blood volume subsequently causes the adventitial layer to delaminate and coagulated blood leads to intramural thrombus formation. In some cases the adventitial delamination leads to additional ruptures of the medial layer near the orifices of the intercostal arteries, which subsequently cause additional intramural hematomas that result in polymorphic aneurysms along the thoracic aorta. In conclusion, our data allow for the first time for a detailed, clear and unequivocal description of the morphology of angiotensin II-induced AAA in mice.